PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#17
Linda
8/29/02

Applicant	:	John A. Arcadi
Application No.	:	09/383,114
Filed	:	August 25, 1999
Title	:	COMPOSITION AND METHOD FOR TREATING CARCINOMA (as amended)
Grp./Div.	:	1614
Examiner	:	J. Goldberg
Docket No.	:	35687/RWJ/H29

DECLARATION

Assistant Commissioner for Patents
Washington, D.C. 20231

Post Office Box 7068
Pasadena, CA 91109-7068

Commissioner:

I, Lawrence W. Jones, declare that:

1. I am a licensed physician in the State of California. I am also the Director of Prostate Research Program at Huntington Medical Research Institutes (HMRI), a non-profit medical research organization and the assignee of the above patent application. I have been working in the field of treating prostate cancer for more than 28 years, and have worked as an unpaid volunteer for HMRI since 1974. I am thoroughly familiar with the patent application, and I have no financial interest in it.

2. The patent application discloses the use of rhodamine-123 for treating hormone-refractory prostate cancer, which kills 40,000 men annually in the United States. Before this invention, there was no known life-prolonging treatment for this disease.

3. I am also familiar with the Office action dated 03/11/02, and with an Amendment filed November 6, 2001 (erroneously referred in the Office action as "filed on O8 January 2002"). The Office action contends that the original disclosure of the patent application does not support certain material added by the Amendment, namely, the word "carcinoma" and the term "one of many carcinomas, such as cancer of the breast, liver, pancreas, bladder, lung, skin, colon, and the like." As explained below,

the material objected to in the Office action, is not "new matter". It merely states the meaning of "carcinoma", as it has long been understood by ordinary workers in the field of oncology.

4. The present patent application, and each of its two parent applications, originally disclosed the treatment of carcinoma. For example, the present application describes in detail how to treat prostate cancer with rhodamine-123. It was well known to physicians and other workers in the field of oncology long before the filing date of the present application that prostate cancer is one form of carcinoma, and that carcinoma is any of the various types of malignant tumor derived from epithelial tissue, including cancer of the breast, liver, pancreas, bladder, lung, skin, and colon, as well as other organs of the human body. See Stedman's Medical Dictionary, 24th Edition, published 1982, page 223, which is attached as Exhibit "A".

5. The patent application, as originally filed, states on page 1, line 24, that "Rh-123 is selectively toxic for carcinoma cells." Accordingly, the patent application as originally filed makes clear to ordinary workers in this field that rhodamine-123 is useful for treating carcinoma, such as prostate cancer.

6. The application also makes it clear how to administer rhodamine-123 safely to patients, so that the efficacy of the drug for treating all types of carcinoma can be determined by routine experiments.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date 7/22/2002 By Lawrence W. Jones, M.D.

Lawrence W. Jones, M.D.

RWJ/mas
Attachment : Exhibit A
RWJ PAS449743.1-*-7/22/02 11:05 AM

ILLUSTRATED
Stedman's MEDICAL DICTIONARY
24TH EDITION

WILLIAMS & WILKINS
Baltimore/London

as a fire extinguisher, and has been used as an anthelmintic, especially against hookworm.

carbon-11 (^{11}C). A cyclotron-produced, positron-emitting radioisotope of carbon with a half-life of 20 minutes.

carbon-12 (^{12}C). The standard of atomic mass, 98.89 per cent of natural carbon.

carbon-13 (^{13}C). A natural isotope, 1.11 per cent of natural carbon.

carbon-14 (^{14}C). A beta-emitter with a half-life of 5730 years, widely used as a tracer in studying various aspects of metabolism, notably photosynthesis; naturally occurring ^{14}C, arising from cosmic rays, is used to date relics containing natural carbonaceous materials.

car'bonate. A salt of carbonic acid; $CO_3=$.

c. dehydratase (EC 4.2.1.1), c. hydro-lyase; carbonic anhydrase; a zinc-containing enzyme in red blood cells that catalyzes the conversion of carbon dioxide (CO_2) entering the blood from the tissues into carbonic acid (H_2CO_3). The reverse reaction occurs when the blood reaches the lungs and carbon dioxide is liberated.

c. hydro-lyase, c. dehydratase.

carbon'ic. Relating to carbon.

carbon'ic acid. H_2CO_3, formed from H_2O and CO_2.

carbon'ic anhy'drase. *Carbonate* dehydratase.

carbon'ic anhy'dride. *Carbon* dioxide (1).

carbon'ium. An organic cation in which the positive charge is on a carbon atom. It is now recommended that carbocation be used as the class name and carbenium (CH_3^+) be used for specific compound names.

car'bonize. To char.

carbonom'eter [L. *carbo* (*carbon-*), coal, + G. *metron*, measure]. An obsolete device for determining the proportion of carbon dioxide in the air or expired breath by the precipitation of calcium carbonate from lime water.

carbonom'etry. Carbometry; an obsolete method for the determination of the presence and the proportion of carbon dioxide by means of the carbonometer.

carbonu'ria. Rarely used term denoting the excretion of carbon dioxide or other carbon compounds in the urine.

car'bonyl. The characteristic group, $-CO-$, of the ketones, aldehydes, and organic acids.

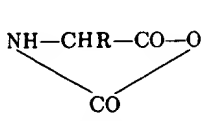
carborun'dum. Carbide of silicon; SiC; a substance of extreme hardness used for polishing in place of emery.

carbox'amide. Aminocarbonyl; a molecular configuration ($-CONH_2$) that, together with the related carboximides (iminocarbonyls) ($-CONH-$), is a constituent of many hypnotics, including barbiturates, hydantoins, and thiazines.

carboxy-. Combining form indicating addition of CO or CO_2.

***N*-carboxyaminoacid anhydrides.** See *N*-carboxyanhydrides.

***N*-carbox'yanhy'drides.** Heterocyclic derivatives of amino acids from which polypeptides may be synthesized.



N-Carboxyanhydride

carbox'ycathop'sin. Dipeptidyl carboxypeptidase.

carbox'ydis'mutase. Ribulosebisphosphate carboxylase.

carbox'yhemoglo'bin (HbCO). Carbon monoxide hemoglobin; a fairly stable union of carbon monoxide with hemoglobin. The formation of c. prevents the normal transfer of carbon dioxide and oxygen during the circulation of blood; thus, increasing levels of c. result in various degrees of asphyxiation, including death.

carbox'yhemoglobine'mia. The presence of carboxyhemoglobin in the blood.

carbox'yl. The characterizing group ($-COOH$) of certain organic acids; *e.g.*, HCOOH (formic acid), CH_3COOH (acetic acid), etc.

carbox'ylase. One of several carboxy-lyases, trivially named carboxylases or decarboxylases (EC group 4.1.1), catalyzing the addition of CO_2 to all or part of another molecule to create an additional $-COOH$ group (*e.g.*, ribulosebisphosphate carboxylase, EC 4.1.1.39).

carboxyla'tion. Addition of CO_2 to an organic acceptor, as in photosynthesis, to yield a $-COOH$ group; catalyzed by carboxylases.

carbox'yltrans'ferases (EC group 2.1.3). Transcarboxylases; enzymes transferring carboxyl groups from one compound to another.

carbox'ypep'tidases. Hydrolases removing the amino acid at the free carboxyl end of a polypeptide chain.

carboxypeptidase A (EC 3.4.17.1). Carboxypolypeptidase; a hydrolase that releases C-terminal amino acids, with exception of arginine, lysine, and proline.

carboxypeptidase B (EC 3.4.17.2). Protaminase; a hydrolase that releases C-terminal lysine or arginine preferentially.

carboxypeptidase C. Acid carboxypeptidase.

carboxypeptidase G. γ-Glutamyl hydrolase.

carboxypolypeptidase. Carboxypeptidase A.

***N*-carbox'yurea.** Allophanic acid.

carbuncle (kar'bung-kl) [L. *carbunculus*, dim. of *carbo*, a live coal, a carbuncle. CARB-]. 1. Deep-seated pyogenic infection of several contiguous hair follicles, with formation of connecting sinuses; often preceded or accompanied by fever, malaise, and prostration. 2. Anthrax (1).

kidney or **renal c.,** severe inflammation within the kidney, usually resulting from the coalescence of multiple intrarenal abscesses into a massive intrarenal nest of infection which may open into the renal pelvis or may extend outward and give rise to perinephric abscess.

carbun'cular. Relating to a carbuncle.

carbunculo'sis. A condition marked by the occurrence of several carbuncles simultaneously or within a short period of time.

car'buret. 1. Archaic for carbide. 2. To combine with carbon. 3. To enrich a gas with volatile hydrocarbons, as in a carburetor.

carbu'tamide. Aminophenurobutane; 1-butyl-3-sulfanilylurea; an oral hypoglycemic agent.

carbu'terol hydrochloride. [5-[2-(*tert*- Butylamino)-1-hydroxyethyl]-2-hydroxyphenyl]urea monohydrochloride; a sympathomimetic drug with bronchodilatory activity.

carcass (kar'kas) [F. *carcasse*, fr. It. *carcassa*]. 1. The body of a dead animal. 2. In butcher's terminology, refers to animals used for human food; the body after the hide, head, tail, extremities, and viscera have been removed.

carcin-. See carcino-.

carcino-, carcin- [G. *karkinos*, crab, cancer. CARC-]. Combining form relating to cancer.

carcinogen (kar'sĭ-no-jen). Any cancer-producing substance. The most potent c.'s, including those isolated from coal tar, are polycyclic aromatic hydrocarbons.

car'cinogen'esis [carcino- + G. *genesis*, generation]. The origin or production of cancer, including carcinomas and other malignant neoplasms.

car'cinogen'ic. Cancerigenic; causing cancer.

car'cinolyt'ic [carcino- + G. *lytikos*, causing a solution]. Destructive to the cells of carcinoma.

CARCINOMA

carcinoma (CA) (kar-sĭ-no'mah) [G. *karkinōma*, fr. *karkinos*, cancer, + suffix *-oma*, tumor]. Any of the various types of malignant neoplasm derived from epithelial tissue in several sites, occurring more frequently in the skin and large intestine in both sexes, the bronchi, stomach, and prostate gland in men, and the breast and cervix in women. C.'s are identified histologically on the basis of invasiveness and the changes that indicate anaplasia, *i.e.*, loss of polarity

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